

## ABSTRACT OF THE DISCLOSURE

The invention provides methods to activate tumor suppressors. The invention further provides antisense oligonucleotides complementary to a portion of the MDM2-encoding RNA and methods for using such antisense oligonucleotides as analytical and diagnostic tools, as potentiators of transgenic animal studies and for gene therapy approaches, and as potential therapeutic agents. The invention also provides methods to augment and synergistically activate a tumor suppressor in conjunction with the use of a DNA-damage inducing agent. The invention further provides *in vitro* and *in vivo* models to evaluate the therapeutic effectiveness of a recently identified anti-human-MDM2 antisense oligonucleotide in the treatment of human colorectal cancers.